UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/786,725	04/23/2001	Hans-Werner Heinrich	101195-44	4120

27387 7590 12/26/2007

NORRIS, MCLAUGHLIN & MARCUS, P.A.
875 THIRD AVE
18TH FLOOR
NEW YORK, NY 10022

EXAMINER
WILLIAMS, KAREN M

ART UNIT	PAPER NUMBER
PCT	

MAIL DATE	DELIVERY MODE
12/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/786,725	HEINRICH ET AL.	
	Examiner	Art Unit	
	James L. Grun	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-15 and 17-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-15 and 17-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 19 October 2007 has been entered. Claims 21 and 22 are newly added. Claims 1, 3-15, 17-22 remain in the case.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

All disclosed sequences, e.g. all the sequences disclosed on pages 4, 5, 7, and 9 and in claims 4, 7, 15, and 17, are not listed in the Sequence Listing as required. The examiner would note that: the sequence disclosed in the specification and claims as SEQ ID NO: 3 is listed in the Sequence Listing as both SEQ ID NO: 3 and SEQ ID NO: 4; the sequence disclosed in the specification and claims as SEQ ID NO: 4 is listed in the Sequence Listing as SEQ ID NO: 5; and, the sequence disclosed in the specification and claims as SEQ ID NO: 5 is not listed in the Sequence Listing. Appropriate correction is required.

Applicants are required to provide a substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification, which includes each of the sequences disclosed in the specification as required by 37 CFR 1.821(c). A substitute copy of

the "Sequence Listing" in computer readable form must be provided as required by 37 CFR 1.821(e). Applicants must direct the entry of proper "SEQ ID NO:" identifiers for every appearance of sequences in the description or claims of the patent application. Applicants must also provide a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter as required by 37 CFR 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g).

The disclosure is objected to because of the following informalities: the specification contains too many grammatical, idiomatic, and spelling errors to list specifically and should be carefully revised. Examples of these include: multiple recitations of "Elastase" rather than --elastase--, "myelome" rather than --myeloma--, "hybridome" rather than --hybridoma--, "immunisation" rather than --immunization--, "common limpet" rather than --Keyhole limpet--, or, "connection places" rather than --binding sites--; page 2, "polyclonalen" should be --polyclonal--, "methods fails" should be corrected; page 4, --all known-- and --a suitable-- should be recited; page 5, "--programs-- and --synthesized-- should be recited; page 6, "bodies" should be --antibodies--; page 7, --antisera-- should be recited; page 9, it is believed --column-- and --precipitation-- were intended. Appropriate correction is required.

Applicant's arguments filed 19 October 2007 have been fully considered but they are not deemed to be persuasive.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

Claims 1, 3-11 and 17-22 are rejected under 35 U.S.C. 112, first paragraph, for reasons of record, that the specification contains subject matter which was not described in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicant's arguments filed 19 October 2007 have been fully considered but they are not deemed to be persuasive.

Applicant urges that elastase assay reagents and steps were known to the art, that the antibody products are not being claimed, only their "novel" use, that applicant provides particular peptides, that applicant elicits antibodies to those particular peptides and thus applicant provides antibodies to all known elastase iso-enzymes which function in the invention as claimed, that disclosure of methods to make antibodies adequately describe and enable the invention as claimed, and that merely stating that monoclonal antibodies are part of the invention is sufficient to describe and enable monoclonal antibodies as claimed.

These arguments are not found persuasive for the extensive reasons of record.

Notwithstanding applicant's assertion to the contrary, specific antibody reagents are claimed in the kit claims, and the method claims also require specific antibody reagents, which must be adequately described and enabled by the disclosure.

Notwithstanding applicant's assertions to the contrary, the ability of one to provide a recited peptide is not at issue. For the reasons of record, the issue is whether the disclosure describes and supports the ability of the peptides to elicit antibodies that bind singly, or in combination, and function for determination of all elastase isoforms in a body fluid sample.

As set forth previously, applicant teaches only polyclonal antibodies to particular peptides and provides no description or guidance to any single antibody or monospecific species which functions in the invention to bind to all known elastase iso-enzymes. As set forth, adequate written description requires more than a mere statement that a product is part of the invention, more than a reference to a potential method of isolating it, and more than a generic statement which defines a genus of products by only their functional activity. As set forth, the product itself is required as well as recitation of a representative number of products falling within the scope of a claimed genus. Moreover, as set forth, all possible analogs of a product are not enabled by a disclosure wherein the characteristics of the analogs are unpredictable. As set forth, a patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. For the reasons of record, and as summarized above, applicant has not described or enabled any antibody which functions **singly** as claimed.

For reasons of record, applicant also provides no guidance for usable combinations. In this regard, as set forth, some of the peptides suggested for use by applicant would be expected

to elicit antibodies that bind to an isoform which corresponds to porcine elastase, which is not expressed in the human pancreas, and which would complicate the assay in certain patient populations. Applicant urges that such cross-reactivity can be eliminated by elimination of an antibody from the combination as taught in the poster of Weiss et al. This is not found persuasive because the argument is not consistent with or commensurate in scope with the invention as disclosed and claimed and does not inform one as to which, if not all, embodiment(s) of applicant's suggested and claimed method is(are) inoperative.

As set forth previously, applicant teaches only polyclonal antibodies to particular peptides and provides no description or guidance to any antibodies or combination of antibodies capable of predictable binding to any or all of the elastase enzyme isoforms as found in stool or body fluid samples, because only binding to proteins in Western blots, i.e. after SDS denaturation, is specifically exemplified. One could not predict the ability of any of the antibodies to the suggested peptides to bind to non-denatured protein as found in a fluid sample from a patient. As set forth, adequate written description requires more than a mere statement that a product is part of the invention, more than a reference to a potential method of isolating it, and more than a generic statement which defines a genus of products by only their functional activity. As set forth, the product itself is required as well as recitation of a representative number of products falling within the scope of a claimed genus. Moreover, as set forth, all possible analogs of a product are not enabled by a disclosure wherein the characteristics of the analogs are unpredictable. As set forth, a patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. As set forth, absent further written description and guidance from applicant, one would have no

assurance of successfully obtaining appropriate functional antibody reagents and predictably performing the method as suggested by applicant.

Notwithstanding applicant's assertions to the contrary, the existence of elastase iso-enzymes and their sequences were well known to the art as taught in, for example, Tani et al. and were not determined by applicant.

Applicant refers to a previously submitted synopsis of publications, some comparing the sensitivity and specificity of a single commercial assay based on the disclosures of the cited prior art publications, particularly that of Scheefers et al., and unspecified embodiments, implicitly of the instant disclosure, as evidence of the "suitability and practicability of the claimed method." This is not found persuasive for a number of reasons. Firstly, it is not even clear what, if any, embodiment(s) of applicant's suggested invention was(were) tested against the prior art assay using the particular monoclonal antibodies taught in Scheefers et al. Secondly, the cited publications would appear to support the examiner's argument that the antibodies, if elicited with applicant's disclosed methods, do not bind to all known elastase iso-enzymes as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-15, and 17-22 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3-5, and 20 involve method claims and, as such, they should clearly set forth the various method steps in a positive, sequential manner using active tense verbs such as mixing, reacting, and detecting. "Employing" or "using" or similar terms are not valid method steps. In these claims, "the antigen" lacks antecedent basis.

In claim 3 and claims dependent thereupon, it is not clear how antibodies are obtained "by means of antigens," e.g. it is not clear what applicant intends as encompassed because it is not clear if the antigens are immunogens, or binders in affinity chromatography, or used in some other means.

In claims 4, 7, 14, 15, and 17, and claims dependent thereupon, "SEQ ID NO:" identifiers are recited that do not correspond to sequences as listed in the Sequence Listing.

In claim 6, "the pancreas" lacks antecedent basis. It is not clear what applicant intends as excluded because the excluded amino acid sequence is of a peptide not an iso-enzyme.

Claims 12-15 each fail to close the parentheses before the period.

In claim 17 and claims dependent thereupon, "the antigen" lacks antecedent basis.

Claim 18 is indefinite in that the claims fail to further limit the subject matter of a previous claim and set forth an intended use but fail to point out what components are included or excluded by the claim language.

In claim 19, the interrelationships of the components are not clear, e.g. it is not clear if hemocyanin is a carrier substance.

In claim 20, the interrelationships of the components are not clear, e.g. it is not clear if peptides are sub-units. It is not clear what is intended by "myeoloma cells" or "hybridoma cells which are cultivated in cell lines."

Claims 21 and 22 claim identical subject matter.

Applicant's arguments filed 19 October 2007 have been fully considered but they are not deemed to be persuasive. Notwithstanding applicant's assertions to the contrary, applicant's amendments have not obviated rejections under this statute for the reasons set forth above. Notwithstanding applicant's assertions to the contrary, the objectionable terms are found in the claims as noted above, including in dependent claims which include the limitations of the claims from which they depend. Notwithstanding applicant's assertions to the contrary, claim 20 has not been cancelled.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-8, 10-15, and 17-22 are rejected under 35 U.S.C. § 102(b) as being anticipated by Scheefers et al. (U.S. Pat. No. 5,622,837) in light of the instant disclosure for reasons of record.

Claims 1, 3-8, 10, 12-15, 17, 18, 21, and 22 are rejected under 35 U.S.C. § 102(b) as being anticipated by Sziegoleit et al. (Clin. Biochem. 22: 79, 1989) in light of the instant disclosure for reasons of record.

Applicant's arguments filed 19 October 2007 have been fully considered but they are not deemed to be persuasive.

Applicant urges that elastase enzymes are digested in the intestinal tract. This is not found persuasive because the argument is contradictory to that which is known in the art and that which is disclosed in the specification, that elastase "displays extraordinary stability during the passage through the intestines" (see Specification, page 2).

Applicant urges that the antibodies of the prior art are specific for a single amino acid sequence. This is not found persuasive for a number of reasons. Firstly, the argument is not found persuasive because the argument is at odds with the invention as instantly claimed in which antibodies specific for a peptide can be used singly. Secondly, notwithstanding applicant's assertions and arguments to the contrary, the disclosures of the references are considered as a whole and: are not limited to only the monoclonal antibody commercial embodiment of the sandwich assay derived from Scheefers et al., monoclonal antibodies which, the examiner would note, are not taught as specific for the peptide as instantly excluded and which may have been produced from the fusion of cells obtained from animals immunized with the purified enzyme (see e.g. Scheefers et al., cols. 2, 3, and 5-6); or, are not limited to only a suggested preferred embodiment. As set forth, Sziegoleit et al. teach elicitation of polyclonal antibodies to purified enzyme and Scheefers et al. teach elicitation of both polyclonal and monoclonal antibodies to purified enzyme and fragments thereof, not only to the suggested antigen/immunogen as instantly excluded, for use in sandwich enzyme-linked immunosorbent assay for diagnosis of pancreatic diseases. As set forth, the enzyme preparation would inherently be a mixture of at least the elastase I isoforms (i.e. elastases IIIA and IIIB), and polyclonal antibodies elicited thereto would inherently bind to the isoforms and cross-react with similar epitopes as found in elastase II. Moreover, the teaching of a preferred peptide does not serve to

teach away from any other fragment of the enzyme as taught for use in Scheefers et al. (see e.g. col. 2).

As set forth, the Patent and Trademark Office does not have the facilities and resources to provide the *factual* evidence needed in order to establish that there is a difference, in the first place, between the reagents of the prior art and those instantly disclosed and, that if there is such a difference, that such a difference would have been considered unexpected, i.e. unobvious, by one of ordinary skill in the art. The burden is upon applicant to present such factual evidence. See e.g. In re Best (195 USPQ 430 (CCPA 1977)) or Ex parte Phillips (28 USPQ2d 1302 (BPAI 1993)). In this regard, applicant refers to a previously submitted synopsis of publications, some comparing the sensitivity and specificity of a single commercial assay based on the disclosures of the cited prior art publications, particularly that of the monoclonal antibodies of Scheefers et al., and unspecified embodiments, implicitly of the instant disclosure, as evidence that the antibodies of the prior art do not bind all isoforms of elastase as found in stool. This is not found persuasive because the only evidence the examiner can find in the abstracts that antibodies do not bind all isoforms of elastase is in regard to antibodies produced by the instant assignee (BIOSERV) implicitly elicited to peptides, and not intact enzyme, using the instantly disclosed methods (see e.g. the abstract of Weiss et al.). Again, the argument is not found persuasive with regard to the polyclonal antibodies to intact purified enzymes or other fragments thereof as taught in the prior art.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, SPE, can be contacted at (571) 272-0823.

The phone number for official facsimile transmitted communications to TC 1600, Group 1640, is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/JLG/
James L. Grun, Ph.D.
December 12, 2007

LONG V. LE 12/13/07
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600